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EXAMINER	
SAKELARIS, SALLY A	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/782,604	GOSWAMI ET AL.
	Examiner	Art Unit
	Sally A Sakelaris	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-73* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8,11,28,32,33,46,52,58,60-66,69,71,76,82 and 83* is/are rejected.

7)☒ Claim(s) *1,11,32,33,76,82 and 83* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims withdrawn from consideration are 5-7,9,10,12-27,29-31,34-45,47-51,53-57,59,67,68,70,72-75,77-81,84 and 85.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, Claims 1-4, 8, 11, 28, 32, 33, 46, 52, 58, 60-66, 69, 71, 76, 82, and 83 and the sequences of SEQ ID NOS: 4, 44, 21 and 22 corresponding to the elected, *Stenobrachis leucopsarus* in the Paper submitted March 6, 2003 is acknowledged. Applicant's arguments filed 3/6/03 have been fully considered but they are not persuasive. The traversal is on the grounds that the examination of only one nucleotide sequence, which would require a separate application for each polynucleotide is believed by applicant to be in violation of MPEP §803.04. First, applicant should note that the examiner did not limit them to a single sequence. Secondly, it is maintained however, that the *Official Gazette* and notices posted on the PTO website have included guidance "to include up to 10 nucleotide sequences per application." The examiner retains her discretion in the inclusion of "up to 10 sequences." It is further maintained that the examiner adhered to the PTO policy concerning restriction practice as defined in *35 U.S.C. 121*, "if two or more independent and distinct inventions are claimed in one application, the commissioner may require the application to be restricted to one of the inventions." The examiner maintains that the inventions are distinct, each from the other because of the following reasons:

These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequences are presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq. Each sequence characteristic to a specific species and genomic region are patentably distinct because they are

unrelated sequences, i.e. these sequences are unrelated because each has a different nucleotide composition and as a result different physical and biochemical properties and differs in structure and in function and in biological activity. The restriction requirement is thus made FINAL.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code(Pg. 9, for example). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s): Claims 11, 32, 33, 76, 82, and 83 contain nucleotide sequence sans identifiers. Additionally, an objection is made to the sequence of claim 82 as it is not clear to which SEQ ID NO: it correlates. The sequence of claim 82 lacks the last "C" of SEQ ID NO: 21.

In order to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825), Applicant must submit a new CRF and paper copy of the Sequence Listing containing these sequences, in addition to the previously listed sequences, an amendment directing the entry of the Sequence Listing into the specification, an amendment directing the insertion of the SEQ ID

NOs into the appropriate pages of the specification and a letter stating that the content of the paper and computer readable copies are the same.

In addition, claim 1 is objected to as roman numeral, "(xiii)" is absent. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 8, 11, 28, 32, 33, 46, 52, 58, 60-66, 69, 71, 76, 82, and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1-4, 8, 11, 28, 32, 33, 46, 52, 58, 60-66, 69, 71, 76, 82, and 83 are indefinite. Claim 1 recites the limitation "the selected primers" in line 4 and "the amplifying" in line 5. There is insufficient antecedent basis for each of these limitations in the claim. It is not clear to which primers and to what "amplifying" step these recitations are referring. Applicant should provide proper antecedent basis for both of these limitations.

B. Claims 4, 11, 32, 33, 46, 52, 58, 66, 69, 71, 82, and 83 all recite the limitation "D-Loop". There is insufficient antecedent basis for each of these limitations in the claim. It is not clear to what these claims are referring, as no "D-Loop" recitation exists in claim 1. Applicant should provide proper antecedent basis for these limitations.

C. Claim 76 recites the limitation of "PSL PROL". There is insufficient antecedent basis for this limitation in the claim. It is not clear what the nucleotide sequence comprised as "PSL PROL" does not have antecedent basis in the claims.

D. Claim 8 is indefinite over the recitation of "20 meu. L." This phrase makes the claim unclear because the specification does not define what unit of measurment is encompassed by "20 meu.L". There is no fixed definition in the art for what constitutes a "meu.L.". It is unclear, eg. whether the term refers to the greek letter "μ" or instead to "mole equivalent units". The claims should be amended to clarify to what specific measurement, "20 meu. L." refers.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-4, 8, 28, 46, 52, 58, 60-66, 69, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foran(J. of Exp. Zoology, 1991) in view of Yamaguchi et al.(Molecular Phylogenetics and Evolution, 2000) in further view of Davidson(WO 92/05277), in even further view of Lee et al(J Mol. Evol. 1995), in even further view of Herrnstadt et al.(US Patent 5,827,657) and in an even further view of Haygood et al.(J. of Exp. Zoology, 1994).

Foran teaches construction of bacterial and Myctophid fish clones to be used as probes. The reference teaches with respect to claim 1: (i) extracting the DNA from the muscle tissue of a myctophid fish, (ix) ligating the Vibrio fischeri Lux clone pJE205, following digestion into Bluescript vector DNA using published protocols(Foran, 2), (xi) and (xii) The reference further teaches that "the ligation mixture was used to transform competent E. coli cells (XL1-blue, Stratagene)"(Foran, 2) and that "plasmid DNAs from transformed bacteria were isolated by the

alkaline lysis method"(Foran, 2). Lastly the reference teaches that "in a similar manner, fragments of fish DNA were cloned for use as positive controls and to help quantitate the relative amount of DNA in a given lane on fish blots"(Foran, 2). It should be noted that included in the reference's teaching of the Bluescript vector DNA(Stratagene Cloning Systems) is the further teaching of the embodiments of claims 60-65, all relating to said system.

Foran does not teach claim 1's steps relating to amplification and cloning included in (ii)-(viii), (x), (xiv)-(xxiv), nor does it teach the method wherein the myctophid fish is from Stenobrachis leucopsarus, or the method wherein the gene regions to be amplified from this fish are mitochondrial in source.

Yamaguchi et al. teach generically, molecular phylogeny and larval morphological diversity of the lanternfish genus Hygophum (Teleostei: Myctophidae)

With respect to claim 1: (i)extracting the DNA from the muscle tissue of a myctophid, of the order Teleostei, fish(Pg. 104), (ii) selecting gene regions in the extracted DNA with the selected primers and the amplifying the same using polymerase chain reaction (PCR), (iii) eluting the PCR amplified DNA(bottom right Pg. 104), (v) cycle sequencing of eluted DNA through use of the Applied Biosystems 373 DNA sequencer, (viii) confirming the sequences for the target gene through alignment programs such as CLUSTAL X and analyzing phylogenetic relationships using maximum-parsimony (MP), maximum-likelihood (ML), and neighbor-joining (NJ) methods(Pg. 105).

With respect to claim 3: Yamaguchi teaches the method above wherein the DNA from the muscle tissue is mitochondrial(Pg. 104).

With respect to claim 28, Yamaguchi teaches the method above wherein the cycle sequencing primer concentration used was 2.5μl(Pg. 104).

Davidson et al. teach: With respect to claim 1: (i) extracting samples of skeletal muscle from different tuna species(Pg. 43) (ii) selecting the gene regions in the extracted DNA with the selected primers and the amplifying the same using polymerase chain reaction (PCR)(Pg. 45) (iii) eluting the PCR amplified DNA by centrifugal dialysis(Pg. 46) (iv)reamplifying the gene regions from PCR amplified DNA and eluting the same(Pg. 47, lines 24-30(2^{nd} PCR) lines 33-Pg. 48 line 4(Eluting)) (v) cycle sequencing the eluted DNA using a single primer(Pg. 49, Ex.1) (vi) purifying extension products through use of DNA Sequencing kit(Pg. 50) (vii) sequencing the extension products on an acrylamide gel(Pg. 50, lines 9-10) (viii)confirming the sequences for the target gene by comparing it to sequences from known species(50), (xxiv) designing species specific primers from the sequences(abstract).

With respect to claim 3: Davidson et al. teach the method above wherein the DNA from the muscle tissue is mitochondrial in source(Pg. 46).

Lee et al. teach: With respect to claim 1: (i)-(viii) total genomic DNA was prepared from muscle tissue of a teleost fish, followed by multiple steps of PCR amplification with primers specific to the mitochondrial control region, specifically, the D-loop region(Pg. 55 *Amplification),* (ix) ligating the eluted PCR product, of an amplified D-loop region from genomic DNA of a teleost fish's muscle tissue(Pg. 55), in a vector, a pBluescript II plasmid and subsequent transformation of ligated plasmid and plating methods followed the manufacturer's(Stratagene) instruction manual,(x)-(xxxiv) are taught inherently in the references

teaching on page 55 of the standard miniprep analysis(Sambrook et al. 1989) and furthermore through their teachings of sequencing and sequence analysis of the miniprepped DNA.

With respect to claim 4, Lee et al. teach the above method wherein the mitochondrial genes amplified belong to the D-loop gene region of fish in the order, Teleost(of which Myctophidae is a member)(Entire document).

Herrnstadt et al. teach collectively, the direct cloning of PCR amplified nucleic acids.

With respect to claim 1: (ix) ligating the eluted PCR products in a vector(Col. 12) (x) preparing the electro-competent cells for electro transformation(Col. 15) (xi) electro transforming the host cells(Col. 15) (xii) growing and harvesting of transformed host cells(Col. 16) (xiv) confirming that the transformed bacteria has the plasmids with the gene inserts by PCR(Col. 19) (xv) purifying recombinant plasmid DNA having the cloned gene probes from the transformed host cells(Col. 19) (xvi)checking purity and specificity of the cloned DNA probe insert by cutting with restriction enzyme(Col. 19) (xvii) confirming the molecular size of the DNA probe insert(Col. 19).

Haygood et al. teaches: With respect to claims 1 and 2: the isolation of genomic DNAs from muscle of the Lanternfish genus, specifically hybridization of gene probes to DNA from muscle and skin of myctophids, namely Stenobrachius leucopsarus(Table 1 and Pg. 227 right side) is taught. Probes are hybridized to the DNA isolated from muscle tissue of Stenobrachius leucopsarus to establish that bioluminescence of Myctophid and Stomiiform fishes is not due to bacterial luciferase.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the reference of Foran in view of Yamaguchi to

analyze the mitochondrial gene of Myctophids since "the genus taught, hygophum is one of 32 genera in the family myctophidae" and as a result will yield similar results to that expected from another species, S. leucoparus. In addition, it would have been obvious to incorporate Blast email in the method of Foran in view of Yamaguchi as it is seen as an equivalent technology to the methods Yamaguchi et al. taught of sequence alignment. It would have also been obvious to alter the concentration of the cycle sequencing primer concentration from 2.5 μl to 2.0 μl, as optimization of PCR is a skill well known in the art. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the reference of Foran in view of Yamaguchi in further view of Davidson to include the steps of claim 1, that although are well known in the art, were not taught by Foran and Yamaguchi but whose combination is motivated by the reference's teaching of a more complete amplification process and cloning regiment for extracted genomic DNA from the muscle tissue of another related fish. It would have also been obvious to repeat the steps (xviii)-(xxiii) including PCR amplification, sequencing and blast emailing as the reference and knowledge in the art, previously taught the use of these steps and their repetition does not make them novel. Davidson et al. also provides the motivation of incorporating their method steps as the ability to probe genetic material, "as well as manipulate genetic material, has increased the need for means to analyze the composition and base order of genetic material…It is therefore desirable to provide for recording various genetic fragments which allow for hybridization with the complementary fragment, so that mixtures may be analyzed for the particular nucleotide sequences"(Pg.8). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the reference of Foran in view of Yamaguchi in further view of Davidson and in even

further view of Lee to have included the amplification of a teleost fish, mitochondrial, D-loop control region as "recently the use of nucleotide sequence data rather than RFLPs, has been encouraged, primarily because of the greater sensitivity of sequencing in detecting variants" and furthermore that "PCR techniques make it feasible to target particular gene segments carrying the highest density of intraspecific variation in large numbers of individuals"(Lee, 54). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the reference of Foran in view of Yamaguchi in further view of Davidson and in even further view of Lee and in an even further view of Herrnstadt et al. as the methods described in the reference for the expected benefit that "sequence information obtained by the present invention will be more reliable than previously available from direct sequencing of PCR amplification products due to more specific ligation reactions and reduced numbers of restriction fragments"(Col. 3). Lastly, It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the reference of Foran in view of Yamaguchi in further view of Davidson and in even further view of Lee and in an even further view of Herrnstadt et al. and in an even further view of Haygood as the reference's teaching of probes to Stenobrachius leucopsarus is an addition to the teachings of Foran who also taught this same method but only to other myctophidae, not to the specifically claimed genus and species of Stenobrachius leucopsarus. As a result, combining the teachings of Foran in view of Yamaguchi in further view of Davidson and in even further view of Lee and in an even further view of Herrnstadt et al. and in an even further view of Haygood would have been obvious at the time the invention was made.

Any inquiry concerning this communication or earlier communication from the examiner should be directed to Sally Sakelaris whose telephone number is (703) 306-0284. The examiner can normally be reached on Monday-Thursday from 7:30AM-5:00PM and Friday from 1:00PM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W.Gary Jones, can be reached on (703)308-1152. The fax number for the Technology Center is (703)305-3014 or (703)305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to Chantae Dessau whose telephone number is (703)605-1237.

Sally Sakelaris

8/08/2003

JEFFREY FREDMAN
PRIMARY EXAMINER